

### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of Claims:**

Claim 1. (Canceled)

Claim 2. (Canceled)

Claim 3. (Original): A method for determining the sensitivity of a proliferative disease in a subject to a combined treatment with an mTOR inhibitor and a cytotoxic agent, comprising determining the status of p53 (TP53) gene and/or the level of expression/post-translational modification of p53 in a sample derived from the subject.

Claim 4. (Currently amended): A method ~~or use~~ according to ~~any preceding claim 3~~, wherein the proliferative disease comprises a cancer.

Claim 5. (Currently amended): A method according to ~~any of claims 3 to 4~~, comprising determining the genetic status of p53 (TP53) and/or the level of expression of p53.

Claim 6. (Currently amended): A method according to ~~any of claims 3 to 5~~, wherein the sample is derived from a tumor in the subject.

Claim 7. (Currently amended): A method of selecting subject suffering from a proliferative disease for a combined treatment with an mTOR inhibitor and a cytotoxic agent, comprising determining the sensitivity of the proliferative disease to the combined treatment in each subject by a method as described in ~~any of claims 3 to 6~~, and selecting those subjects showing wild-type p53 (TP53) status for the combined treatment.

Claim 8. (Currently amended): A method ~~or use~~ according to ~~any preceding claim 3~~, wherein the mTOR inhibitor comprises rapamycin or a rapamycin derivative.

Claim 9. (Currently amended): A method ~~or use~~ according to claim 8, wherein the rapamycin derivative comprises 40-O-(2-hydroxyethyl) rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin or 40-epi-(tetrazolyl)-rapamycin.

Claim 10. (Currently amended): A method ~~or use~~ according to ~~any preceding claim 3~~, wherein the cytotoxic agent is selected from an antineoplastic antimetabolite, a platin compound, an alkylating agent, a topoisomerase I or II inhibitor, a microtubule active agent and irradiation.

Claim 11. (Canceled)

Claim 12. (Canceled)

Claim 13. (Original): A method for determining the sensitivity or response of a proliferative disease in a subject to a treatment with an mTOR inhibitor in combination with a cytotoxic agent, comprising determining in a sample derived from the subject the level of p21 expression after treatment with the cytotoxic agent along and after a combined treatment of the cytotoxic agent with an mTOR inhibitor.

Claim 14. (Original): A method for enhancing the activity of a cytotoxic agent or for overcoming resistance to a cytotoxic agent in a subject treated with said cytotoxic agent, comprising

- determining the level of p21 expression in a sample derived from the subject,
- if p21 expression is upregulated after administration of a cytotoxic agent, administering to said subject a therapeutically effective amount of an mTOR inhibitor in combination with the cytotoxic agent,
- determining again the level of p21 expression in a new sample derived from the subject after the treatment with the combination of the mTOR inhibitor and the cytotoxic agent, and
- if p21 expression is downregulated, further treating the subject with the mTOR inhibitor either concomitantly or sequentially with said cytotoxic agent.